

Clinical trial results:

Phase II, Open Label, Single Arm Study Assessing the Clinical Benefit of SAR125844, Administered as Single Agent by Weekly Intravenous (IV) Infusion, for the Treatment of Patients With Advanced Pretreated Non-Small Cell Lung Cancer (NSCLC) Harboring MET Gene Amplification Summary

EudraCT number	2014-005696-93	
Trial protocol	BE HU DE ES NL CZ GR FR AT PL IT	
Global end of trial date	05 January 2016	
Results information		
Result version number	v1 (current)	
This version publication date	05 January 2017	
First version publication date	05 January 2017	
Trial information		

Trial identification	
Sponsor protocol code	ACT14205
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02435121
WHO universal trial number (UTN)	U1111-1163-1136
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Notes:

Sponsors		
Sponsor organisation name	Sanofi aventis recherche & développement	
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380	
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com	
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com	

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage		
Analysis stage	Final	
Date of interim/final analysis	23 February 2016	
Is this the analysis of the primary completion data?	No	
Global end of trial reached?	Yes	
Global end of trial date	05 January 2016	
Was the trial ended prematurely?	Yes	

Notes:

General information about the trial

Main objective of the trial:

To determine the objective response rate (ORR), according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 reviewed by an Independent Third Party Review, of SAR125844 in subjects with advanced pretreated NSCLC harboring MET gene amplification.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.

Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	09 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 1 site in Belgium from 09 November 2015 to 05 January 2016.

Pre-assignment

Screening details:

Out of 153 subjects pre-screened, only 1 subject was enrolled and treated in the study. This subject discontinued due to disease progression (DP) and considered as completed (as per protocol).

Period 1	
Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Arm title	SAR125844
Arm description:	
SAR125844 570 mg/m^2 intravenous (IV) infusion over 3 hours once weekly in each cycle (each cycle 3 weeks) until unacceptable toxicity, DP, or consent withdrawal.	
Arm type	Experimental
Investigational medicinal product name	SAR125844
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SAR125844 570 mg/m² once weekly.

Number of subjects in period 1	SAR125844
Started	1
Treated	1
Completed	1

Baseline characteristics

Reporting groups

	Reporting group title	SAR125844

Reporting group description:

SAR125844 570 mg/m 2 intravenous (IV) infusion over 3 hours once weekly in each cycle (each cycle of 3 weeks) until unacceptable toxicity, DP, or consent withdrawal.

Reporting group values	SAR125844	Total	
Number of subjects	1	1	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1	1	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	0	0	

End points

End points reporting groups

Reporting group title	SAR125844

Reporting group description:

SAR125844 570 mg/m^2 intravenous (IV) infusion over 3 hours once weekly in each cycle (each cycle of 3 weeks) until unacceptable toxicity, DP, or consent withdrawal.

Primary: Percentage of Subjects With Objective Response

End point title	Percentage of Subjects With Objective Response ^[1]
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End point description:

Objective response rate was defined as the percentage of subjects from the assessed population with complete response (CR) or partial response (PR) according to the RECIST version 1.1. CR was defined as disappearance of all target and non-target lesions and normalization of tumor marker level. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. An objective response was confirmed at least 4 weeks after the first documentation of response.

End point type	Primary
zna pome cype	1

End point timeframe:

Baseline up to DP, death or study cut-off, whichever came first (maximum duration: 58 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0 ^[2]		
Units: percentage of subjects			
number (confidence interval 95%)	(to)		

Notes:

[2] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

DOR was defined as the time (in weeks) from the first documentation of objective tumor response (CR or PR) that was subsequently confirmed, to the first documentation of DP or death (due to any cause), whichever occurred first. In the absence of DP or death, the DOR should be censored at the date of the last tumor assessment or the cutoff date, whichever occurs first.

End point type	Secondary
-	

End point timeframe:

From the time of the first documented evidence of a confirmed CR or PR until DP, death or study cut-off, whichever came first (maximum duration: 58 days)

End point type	Secondary		
End point timeframe:			
Baseline up to death or study cut-off date	e, whichever came first (maximum duration: 58 days)		

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0 ^[5]		
Units: months			
median (confidence interval 95%)	(to)		

Notes:

[5] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) for SAR125844			
End point title	Maximum Observed Plasma Concentration (Cmax) for SAR125844		
End point description:			
End point type	Secondary		
End point timeframe:	·		
Day 1 of Cycle 1: 5 minutes hours and 45 hours after E	s before the end of infusion (EOI), 15 minutes, 1 hour, 2.5 to 3 hours, 4		

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0[6]		
Units: mcg/mL			
arithmetic mean (standard deviation)	()		

Notes:

[6] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve (AUC) for SAR125844			
End point title Area Under the Concentration-Time Curve (AUC) for SAR125844			
End point description:	•		
End point type	Secondary		

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI, 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0 ^[7]		
Units: mcg*h/mL			
arithmetic mean (standard deviation)	()		

Notes:

[7] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) for SAR125844 End point title Clearance (CL) for SAR125844 End point description:

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI, 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0[8]		
Units: Litre/hour			
arithmetic mean (standard deviation)	()		

Notes:

[8] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State (Vss) for SAR125844				
End point title	Volume of Distribution at Steady State (Vss) for SAR125844			
End point description:				

End point type	Secondary
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End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI, 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

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End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	O _[ə]		
Units: Litre			
arithmetic mean (standard deviation)	()		

Notes:

[9] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) for SAR125844

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End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) for SAR125844
End point description:	
End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI, 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0[10]		
Units: Hours			
median (full range (min-max))	(to)		

Notes:

[10] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (EORTC QLQ-C30) at Day 1 of Each Cycle and at End of Treatment (EOT)

Change From Baseline in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire
(EORTC QLQ-C30) at Day 1 of Each Cycle and at End of Treatment (EOT)

End point description:

The EORTC QLQ-C30 is a 30-item questionnaire to assess the overall quality of life in cancer subjects. It includes five functional scales (physical, role, cognitive, emotional, and social), global health status/quality of life, disease/treatment related symptoms scales (fatigue, pain, nausea/vomiting) and

other single items (dyspnea, appetite loss, constipation, insomnia, diarrhoea and financial difficulties). 28 questions used 4 point scale (1 "Not at all" to 4 "Very much"); 2 questions used 7-point scale (1 "Very poor" to 7 "Excellent"). Scores were averaged and transformed to 0-100 scale; higher scores indicated better level of functioning or greater degree of symptoms.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), then Day 1 of each cycle (before SAR125844 administration) and at EOT (30 days after last dose) (maximum duration: 58 days)

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0 ^[11]		
Units: units on a scale			
arithmetic mean (standard deviation)	()		

Notes:

[11] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EORTC Quality of Life Questionnaire-Lung Cancer 13 (QLQ-LC13) Score at Day 1 of Each Cycle and at EOT

End point title	Change From Baseline in EORTC Quality of Life Questionnaire-
	Lung Cancer 13 (QLQ-LC13) Score at Day 1 of Each Cycle and
	at EOT

End point description:

QLQ-LC13 consisted of 13 questions relating to disease symptoms specific to lung cancer and treatment side effects typical of treatment with chemotherapy and radiotherapy experienced during past 1 week. The 13 questions comprised 1 multi-item scale for dyspnea and 10 single-item symptoms and side effects (coughing, hemoptysis, sore mouth, dysphagia, peripheral neuropathy, alopecia, chest pain, arm pain, other pain, and medicine for pain). Response ranges from 1 "not at all" to 4 "very much". Scores for each item were transformed to 0 to 100 , where higher symptom score = greater degree of symptoms.

End point type	Secondary
	,

End point timeframe:

Baseline (Day 1 of Cycle 1), then Day 1 of each cycle (before SAR125844 administration) and at EOT (30 days after last dose) (maximum duration: 58 days)

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0 ^[12]		
Units: units on a scale			
arithmetic mean (standard deviation)	()		

Notes:

[12] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cancer Therapy Satisfaction Questionnaire (CTSQ) Score at Day 1 of Cycle 4 and at EOT

End point title	Change From Baseline in Cancer Therapy Satisfaction
·	Questionnaire (CTSQ) Score at Day 1 of Cycle 4 and at EOT

End point description:

CTSQ is a validated 16-item questionnaire that measures three domains related to subject's satisfaction with cancer therapy. These include expectations of therapy (5 questions), feelings about side effects (4 questions), and satisfaction with therapy (7 questions). All questions were assessed on a 5-point scale; 1=never to 5=always. Scores from all questions were averaged and transformed to provide a total score range of 0-100; where higher scores represent better health.

	End point type	Secondary
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End point timeframe:

Baseline (Day 1 of Cycle 1), then Day 1 of Cycle 4 (before SAR125844 administration) and at EOT (30 days after last dose) (maximum duration: 58 days)

End point values	SAR125844		
Subject group type	Reporting group		
Number of subjects analysed	0 ^[13]		
Units: units on a scale			
arithmetic mean (standard deviation)	()		

Notes:

[13] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (58 days) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are treatment emergent that is AEs that developed/worsened that occurred during 'the treatment emergent period' (time from first dose of study drug until 30 days after the last administration of study drug).

Assessment type	Systematic	
Dictionary used		
Dictionary name	MedDRA	
Dictionary version	18.1	
Reporting groups		
Reporting group title	SAR125844	

Reporting group description:

SAR125844 570 mg/m^2 IV infusion over 3 hours once weekly in each cycle (each cycle of 3 weeks) until unacceptable toxicity, DP, or consent withdrawal.

Serious adverse events	SAR125844	
Total subjects affected by serious adverse events		
subjects affected / exposed	1 / 1 (100.00%)	
number of deaths (all causes)	1	
number of deaths resulting from adverse events		
General disorders and administration site conditions		
Disease progression		
subjects affected / exposed	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 1	
deaths causally related to treatment / all	0 / 1	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	SAR125844	
Total subjects affected by non-serious adverse events		
subjects affected / exposed	1 / 1 (100.00%)	
Nervous system disorders		
Dysgeusia		
subjects affected / exposed	1 / 1 (100.00%)	
occurrences (all)	1	

1 / 1 (100.00%)		
1		
1 / 1 (100.00%)		
1		
1 / 1 (100.00%)		
1		
	1 / 1 (100.00%)	1 1 (100.00%)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 November 2015	The study was terminated prematurely due to unsatisfactory subject recruitment.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None of the endpoints were analysed as the study was terminated prematurely due to unsatisfactory subject recruitment.

Notes:

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